

13 R PCT/PTO 14 FEB 2002, 09/555275

SEQUENCE LISTING

<110>	Commonwealth	Scientific	and	Industria1	Research	Organisation
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- <120> Method of Designing Agonists and Antagonists to IGF Receptor
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- <140> 09/555,275
- <141> 2000-05-26
- <150> PCT/AU98/00998
- <151> 1998-11-27
- <150> PP2598
- <151> 1998-03-25
- <150> PP0585
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- Leu Ile Ser Lys Ala Glu Asp Tyr Arg Ser Tyr Arg Phe Pro Lys Leu 35 40 45
- Thr Val Ile Thr Glu Tyr Leu Leu Leu Phe Arg Val Ala Gly Leu Glu 50 55 60
- Ser Leu Gly Asp Leu Phe Pro Asn Leu Thr Val Ile Arg Gly Trp Lys 65 70 75 80
- Leu Phe Tyr Asn Tyr Ala Leu Val Ile Phe Glu Met Thr Asn Leu Lys
 85 90 95
- Asp Ile Gly Leu Tyr Asn Leu Arg Asn Ile Thr Arg Gly Ala Ile Arg
 100 105 110

Ile Glu Lys Asn Ala Asp Leu Cys Tyr Leu Ser Thr Val Asp Trp Ser 115 120 125

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Pro Lys Glu Cys Gly Asp 145 150

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Leu Thr Arg Leu His Glu Leu Glu Asn Cys Ser Val Ile Glu Gly His 20 25 30

Leu Gln Ile Leu Leu Met Phe Lys Thr Arg Pro Glu Asp Phe Arg Asp 35 40 45

Leu Ser Phe Pro Lys Leu Ile Met Ile Thr Asp Tyr Leu Leu Leu Phe 50 55 60

Arg Val Tyr Gly Leu Glu Ser Leu Lys Asp Leu Phe Pro Asn Leu Thr 65 70 75 80

Val Ile Arg Gly Ser Arg Leu Phe Phe Asn Tyr Ala Leu Val Ile Phe 85 90 95

Glu Met Val His Leu Lys Glu Leu Gly Leu Tyr Asn Leu Met Asn Ile 100 105 110

Thr Arg Gly Ser Val Arg Ile Glu Lys Asn Asn Glu Leu Cys Tyr Leu 115 120 125

Ala Thr Ile Asp Trp Ser Arg Ile Leu Asp Ser Val Glu Asp Asn His 130 $\,$ 135 $\,$ 140

Met Arg Asn Leu Gln Glu Ile Leu His Gly Ala Val Arg Phe Ser Asn

Asn Pro Ala Leu Cys Asn Val Glu Ser Ile Gln Trp Arg Asp Ile Val

120

135

115

130

Ile Val Leu Asn Lys Asp Asp Asn Glu Glu Cys Gly Asp

150

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Thr Asp Leu His Ala Phe Glu Asn Leu Glu Ile Ile Arg Gly Arg Thr 85 90 95

Lys Gln His Gly Gln Phe Ser Leu Ala Val Val Ser Leu Asn Ile Thr $100 \hspace{1.5cm} 105 \hspace{1.5cm} 110$

Ser Leu Gly Leu Arg Ser Leu Lys Glu Ile Ser Asp Gly Asp Val Ile 115 120 125

Ile Ser Gly Asn Lys Asn Leu Cys Tyr Ala Asn Thr Ile Asn Trp Lys 130 135 140

Lys Leu Phe Gly Thr Ser Gly Gln Lys Thr Lys Ile Ile Ser Asn Arg 145 150 155 160

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Leu Gly Leu Ile Glu Glu Ile Ser Gly Tyr Leu Lys Ile Arg Arg Ser 50 55 60

Tyr Ala Leu Val Ser Leu Ser Phe Phe Arg Lys Leu Arg Leu Ile Arg 65 70 75 80

Gly Glu Thr Leu Glu Ile Gly Asn Tyr Ser Phe Tyr Ala Leu Asp Asn 85 90 95

Gln Asn Leu Arg Gln Leu Trp Asp Trp Ser Lys His Asn Leu Thr Ile 100 105 110

Thr Gln Gly Lys Leu Phe Phe His Tyr Asn Pro Lys Leu Cys Leu Ser 115 120 125

Glu Ile His Lys Met Glu Glu Val Ser Gly Thr Lys Gly Arg Gln Glu 130 135 140

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Asn

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Met Gly Leu Ile Glu Val Val Thr Gly Tyr Val Lys Ile Arg His Ser 50 55 60

His Ala Leu Val Ser Leu Ser Phe Leu Lys Asn Leu Arg Leu Ile Leu 65 70 75 80

Gly Glu Glu Glu Glu Gly Asn Tyr Ser Phe Tyr Val Leu Asp Asn 85 90 95

Gln Asn Leu Gln Gln Leu Trp Asp Trp Asp His Arg Asn Leu Thr Ile 100 105 110

Lys Ala Gly Lys Met Tyr Phe Ala Phe Asn Pro Lys Leu Cys Val Ser 115 120 125

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Lys Gly Asp Ile Asn Thr Arg Asn Asn Gly Glu Arg Ala Ser Cys Glu 145 150 155 160

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Gln Lys Met Cys Pro Ser Thr Cys Gly Lys Arg Ala Cys Thr Glu Asn 35 40 45

Asn Glu Cys Cys His Pro Glu Cys Leu Gly Ser Cys Ser Ala Pro Asp 50 55 60

Asn Asp Thr Ala Cys Val Ala Cys Arg His Tyr Tyr Tyr Ala Gly Val 65 70 75 80

Cys Val Pro Ala Cys Pro Pro Asn Thr Tyr Arg Phe Glu Gly Trp Arg 85 90 95

Cys Val Asp Arg Asp Phe Cys Ala Asn Ile Leu Ser Ala Glu Ser Ser 100 105 110

Asp Ser Glu Gly Phe Val Ile His Asp Gly Glu Cys Met Gln Glu Cys 115 120 125

Pro Ser Gly Phe Ile Arg Asn Gly Ser Gln Ser Met Tyr Cys Ile Pro 130 135 140

Cys Glu Gly Pro Cys Pro 145 150

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Val Ile Asn Gly Gln Phe Val Glu Arg Cys Trp Thr His Ser His Cys 20 25 30

Gln Lys Val Cys Pro Thr Ile Cys Lys Ser His Gly Cys Thr Ala Glu 35 40 45

Gly Leu Cys Cys His Ser Glu Cys Leu Gly Asn Cys Ser Gln Pro Asp 50 55 60

Asp Pro Thr Lys Cys Val Ala Cys Arg Asn Phe Tyr Leu Asp Gly Arg 65 70 75 80

Cys Val Glu Thr Cys Pro Pro Pro Tyr Tyr His Phe Gln Asp Trp Arg 85 90 95

Cys Val Asn Phe Ser Phe Cys Gln Asp Leu His His Lys Cys Lys Asn 100 105 110

Ser Arg Arg Gln Gly Cys His Gln Tyr Val Ile His Asn Asn Lys Cys 115 120 125

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Gly Arg Cys Arg Gly Lys Ser Pro Ser Asp Cys Cys His Asn Gln Cys

Ala Ala Gly Cys Thr Gly Pro Arg Glu Ser Asp Cys Leu Val Cys Arg 50 55 60

Lys Phe Arg Asp Glu Ala Thr Cys Lys Asp Thr Cys Pro Pro Leu Met 65 70 75 80

Leu Tyr Asn Pro Thr Thr Tyr Gln Met Asp Val Asn Pro Glu Gly Lys 85 90 95

Tyr Ser Phe Gly Ala Thr Cys Val Lys Lys Cys Pro Arg Asn Tyr Val 100 105 110

Val Thr Asp His Gly Ser Cys Val Arg Ala Cys Gly Ala Asp Ser Tyr 115 120 125

Glu Met Glu Glu Asp Gly Val Arg Lys Cys Lys Lys Cys Glu Gly Pro 130 135

Cys Arg 145

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Val Asp Lys Cys Lys Leu Leu Glu Gly Glu Pro Arg Glu Phe Val Glu 35 40 45

Asn Ser Glu Cys Ile Gln Cys His Pro Glu Cys Leu Pro Gln Ala Met 50 60

Asn Ile Thr Cys Thr Gly Arg Gly Pro Asp Asn Cys Ile Gln Cys Ala 65 70 75 80

His Tyr Ile Asp Gly Pro His Cys Val Lys Thr Cys Pro Ala Gly Val 85 90 95

Met Gly Glu Asn Asn Thr Leu Val Trp Lys Tyr Ala Asp Ala Gly His
100 105 110

Val Cys His Leu Cys His Pro Asn Cys Thr Tyr Gly Cys Thr Gly Pro 115 120 125

Gly Leu Glu Gly Cys Pro Thr Asn Gly Pro Lys Ile Pro Ser 130 135 140

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Lys Arg Leu Glu Asn Cys Thr Val Ile Glu Gly Tyr Leu His Ile Leu 20 25 30

Leu Ile Ser Lys Ala Glu Asp Tyr Arg Ser Tyr Arg Phe Pro Lys Leu 35 40 45

Thr Val Ile Thr Glu Tyr Leu Leu Phe Arg Val Ala Gly Leu Glu 50 55 60

Ser Leu Gly Asp Leu Phe Pro Asn Leu Thr Val Ile Arg Gly Trp Lys 65 70 75 80

Leu Phe Tyr Asn Tyr Ala Leu Val Ile Phe Glu Met Thr Asn Leu Lys 85 90 95

Asp Ile Gly Leu Tyr Asn Leu Arg Asn Ile Thr Arg Gly Ala Ile Arg
100 105 110

Ile Glu Lys Asn Ala Asp Leu Cys Tyr Leu Ser Thr Val Asp Trp Ser 115 120 125

Leu Ile Leu Asp Ala Val Ser Asn Asn Tyr Ile Val Gly Asn Lys Pro

130 135 140

Pro Lys Glu Cys Gly Asp Leu Cys Pro Gly Thr Met Glu Glu Lys Pro 145 150 150

Met Cys Glu Lys Thr Thr Ile Asn Asn Glu Tyr Asn Tyr Arg Cys Trp 165 170 175

Thr Thr Asn Arg Cys Gln Lys Met Cys Pro Ser Thr Cys Gly Lys Arg 180 185 190

Ala Cys Thr Glu Asn Asn Glu Cys Cys His Pro Glu Cys Leu Gly Ser 195 200 205

Cys Ser Ala Pro Asp Asn Asp Thr Ala Cys Val Ala Cys Arg His Tyr 210 215 220

Tyr Tyr Ala Gly Val Cys Val Pro Ala Cys Pro Pro Asn Thr Tyr Arg 225 230 235 240

Phe Glu Gly Trp Arg Cys Val Asp Arg Asp Phe Cys Ala Asn Ile Leu 245 250 255

Ser Ala Glu Ser Ser Asp Ser Glu Gly Phe Val Ile His Asp Gly Glu 260 265 270

Cys Met Gln Glu Cys Pro Ser Gly Phe Ile Arg Asn Gly Ser Gln Ser 275 280 285

Met Tyr Cys Ile Pro Cys Glu Gly Pro Cys Pro Lys Val Cys Glu Glu 290 295 300

Glu Lys Lys Thr Lys Thr Ile Asp Ser Val Thr Ser Ala Gln Met Leu 305 310 315 320

Gln Gly Cys Thr Ile Phe Lys Gly Asn Leu Leu Ile Asn Ile Arg Arg 325 330 335

Gly Asn Asn Ile Ala Ser Glu Leu Glu Asn Phe Met Gly Leu Ile Glu 340 345 350

Val Val Thr Gly Tyr Val Lys Ile Arg His Ser His Ala Leu Val Ser 355 360 365

Leu Ser Phe Leu Lys Asn Leu Arg Leu Ile Leu Gly Glu Glu Gln Leu 370 375 380

Glu Gly Asn Tyr Ser Phe Tyr Val Leu Asp Asn Gln Asn Leu Gln Gln 385 390 395 400

Leu Trp Asp Trp Asp His Arg Asn Leu Thr Ile Lys Ala Gly Lys Met 405 410 415

Tyr Phe Ala Phe Asn Pro Lys Leu Cys Val Ser Glu Ile Tyr Arg Met 420 425 430

Glu Glu Val Thr Gly Thr Lys Gly Arg Gln Ser Lys Gly Asp Ile Asn 435 440 445

Thr Arg Asn Asn Gly Glu Arg Ala Ser Cys Glu Ser Asp Val Leu His 450 455 460

Phe Thr Ser Thr Thr Thr Ser Lys Asn Arg Ile Ile Ile Thr Trp His 465 470 475 480

Arg Tyr Arg Pro Pro Asp Tyr Arg Asp Leu Ile Ser Phe Thr Val Tyr 485 490 495

Tyr Lys Glu Ala Pro Phe Lys Asn Val Thr Glu Tyr Asp Gly Gln Asp 500 505 510

Ala Cys Gly Ser Asn Ser Trp Asn Met Val Asp Val Asp Leu Pro Pro 515 520 525

Asn Lys Asp Val Glu Pro Gly Ile Leu Leu His Gly Leu Lys Pro Trp 530 540

Thr Gln Tyr Ala Val Tyr Val Lys Ala Val Thr Leu Thr Met Val Glu 545 550 560

Asn Asp His Ile Arg Gly Ala Lys Ser Glu Ile Leu Tyr Ile Arg Thr 565 570 575

Asn Ala Ser Val Pro Ser Ile Pro Leu Asp Val Leu Ser Ala Ser Asn 580 585 590

Ser Ser Ser Gln Leu Ile Val Lys Trp Asn Pro Pro Ser Leu Pro Asn 595 600 605

Gly Asn Leu Ser Tyr Tyr Ile Val Arg Trp Gln Arg Gln Pro Gln Asp 610 620

Gly Tyr Leu Tyr Arg His Asn Tyr Cys Ser Lys Asp Lys Ile Pro Ile 625 630 635

Arg Lys Tyr Ala Asp Gly Thr Ile Asp Ile Glu Glu Val Thr Glu Asn 645 650 655

Pro Lys Thr Glu Val Cys Gly Glu Lys Gly Pro Cys Cys Ala Cys 660 665 670

Pro Lys Thr Glu Ala Glu Lys Gln Ala Glu Lys Glu Glu Ala Glu Tyr 675 680 685

Arg Lys Val Phe Glu Asn Phe Leu His Asn Ser Ile Phe Val Pro Arg 690 695 700

Pro Glu Arg Lys Arg Arg Asp Val Met Gln Val Ala Asn Thr Thr Met 705 710 715 720

Ser Ser Arg Ser Arg Asn Thr Thr Ala Ala Asp Thr Tyr Asn Ile Thr 725 730 735

Asp Pro Glu Glu Leu Glu Thr Glu Tyr Pro Phe Phe Glu Ser Arg Val 740 745 750

Asp Asn Lys Glu Arg Thr Val Ile Ser Asn Leu Arg Pro Phe Thr Leu 755 760 765

Tyr Arg Ile Asp Ile His Ser Cys Asn His Glu Ala Glu Lys Leu Gly 770 775 780

Cys Ser Ala Ser Asn Phe Val Phe Ala Arg Thr Met Pro Ala Glu Gly 785 790 795 800

Ala Asp Asp Ile Pro Gly Pro Val Thr Trp Glu Pro Arg Pro Glu Asn 805 810 815

Ser Ile Phe Leu Lys Trp Pro Glu Pro Glu Asn Pro Asn Gly Leu Ile 825

Leu Met Tyr Glu Ile Lys Tyr Gly Ser Gln Val Glu Asp Gln Arg Glu 840

Cys Val Ser Arg Gln Glu Tyr Arg Lys Tyr Gly Gly Ala Lys Leu Asn 855

Arg Leu Asn Pro Gly Asn Tyr Thr Ala Arg Ile Gln Ala Thr Ser Leu 875

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Leu Gln Ile Leu Leu Met Phe Lys Thr Arg Pro Glu Asp Phe Arg Asp 35 40

Leu Ser Phe Pro Lys Leu Ile Met Ile Thr Asp Tyr Leu Leu Phe

Arg Val Tyr Gly Leu Glu Ser Leu Lys Asp Leu Phe Pro Asn Leu Thr

Val Ile Arg Gly Ser Arg Leu Phe Phe Asn Tyr Ala Leu Val Ile Phe 85 90

Glu Met Val His Leu Lys Glu Leu Gly Leu Tyr Asn Leu Met Asn Ile 100 105

Thr Arg Gly Ser Val Arg Ile Glu Lys Asn Asn Glu Leu Cys Tyr Leu 115 120 125

Ala Thr Ile Asp Trp Ser Arg Ile Leu Asp Ser Val Glu Asp Asn Tyr 130 135 140

Ile Val Leu Asn Asp Asp Asn Glu Glu Cys Gly Asp Ile Cys Pro Gly 145 150 155 160

Thr Ala Lys Gly Lys Thr Asn Cys Pro Ala Thr Val Ile Asn Gly Gln 165 170 175

Phe Val Glu Arg Cys Trp Thr His Ser His Cys Gln Lys Val Cys Pro 180 185 190

Thr Ile Cys Lys Ser His Gly Cys Thr Ala Glu Gly Leu Cys Cys His 195 200 205

Ser Glu Cys Leu Gly Asn Cys Ser Gln Pro Asp Asp Pro Thr Lys Cys 210 215 220

Val Ala Cys Arg Asn Phe Tyr Leu Asp Gly Arg Cys Val Glu Thr Cys 225 230 235 240

Pro Pro Pro Tyr Tyr His Phe Gln Asp Trp Arg Cys Val Asn Phe Ser 245 250 255

Phe Cys Gln Asp Leu His His Lys Cys Lys Asn Ser Arg Arg Gln Gly 260 265 270

Cys His Gln Tyr Val Ile His Asn Asn Lys Cys Ile Pro Glu Cys Pro 275 280 285

Ser Gly Tyr Thr Met Asn Ser Ser Asn Leu Leu Cys Thr Pro Cys Leu 290 295 300

Gly Pro Cys Pro Lys Val Cys His Leu Leu Glu Gly Glu Lys Thr I1e 305 310 315 320

Asp Ser Val Thr Ser Ala G1n G1u Leu Arg G1y Cys Thr Val Ile Asn 325 330 335

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Ile Arg Arg Ser Tyr Ala Leu Val Ser Leu Ser Phe Phe Arg Lys Leu 370 375 380

Arg Leu Ile Arg Gly Glu Thr Leu Glu Ile Gly Asn Tyr Ser Phe Tyr 385 390 395 400

Ala Leu Asp Asn Gln Asn Leu Arg Gln Leu Trp Asp Trp Ser Lys His
405 410 415

Asn Leu Thr Ile Thr Gln Gly Lys Leu Phe Phe His Tyr Asn Pro Lys 420 425 430

Leu Cys Leu Ser Glu Ile His Lys Met Glu Glu Val Ser Gly Thr Lys 435 440 445

Gly Arg Gln Glu Arg Asn Asp Ile Ala Leu Lys Thr Asn Gly Asp Gln 450 460

Ala Ser Cys Glu Asn Glu Leu Leu Lys Phe Ser Tyr Ile Arg Thr Ser 465 470 475 480

Phe Asp Lys Ile Leu Leu Arg Trp Glu Pro Tyr Trp Pro Pro Asp Phe 485 490 495

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Thr Val Val Asp Ile Asp Pro Pro Leu Arg Ser Asn Asp Pro Lys Ser 530 535 540

Gln Asn His Pro Gly Trp Leu Met Arg Gly Leu Lys Pro Trp Thr Gln 545 550 555

Tyr Ala Ile Phe Val Lys Thr Leu Val Thr Phe Ser Asp Glu Arg Arg 565 570 575

Thr Tyr Gly Ala Lys Ser Asp Ile Ile Tyr Val Gln Thr Asp Ala Thr 580 585 590

Asn Pro Ser Val Pro Leu Asp Pro Ile Ser Val Ser Asn Ser Ser Ser 595 600 605

Gln Ile Ile Leu Lys Trp Lys Pro Pro Ser Asp Pro Asn Gly Asn Ile 610 615 620

Thr His Tyr Leu Val Phe Trp Glu Arg Gln Ala Glu Asp Ser Glu Leu 625 630 635 640

Phe Glu Leu Asp Tyr Cys Leu Lys Gly Leu Lys Leu Pro Ser Arg Thr $645 \hspace{1.5cm} 650 \hspace{1.5cm} 655$

Trp Ser Pro Pro Phe Glu Ser Glu Asp Ser Gln Lys His Asn Gln Ser 660 665 670

Glu Tyr Glu Asp Ser Ala Gly Glu Cys Cys Ser Cys Pro Lys Thr Asp 675 680 685

Ser Gln Ile Leu Lys Glu Leu Glu Glu Ser Ser Phe Arg Lys Thr Phe 690 695 700

Glu Asp Tyr Leu His Asn Val Val Phe Val Pro Arg Pro Ser Arg Lys
705 710 715 720

Arg Arg Ser Leu Gly Asp Val Gly Asn Val Thr Val Ala Val Pro Thr 725 730 735

Val Ala Ala Phe Pro Asn Thr Ser Ser Thr Ser Val Pro Thr Ser Pro 740 745 750

Glu Glu His Arg Pro Phe Glu Lys Val Val Asn Lys Glu Ser Leu Val 755 760 765

Ile Ser Gly Leu Arg His Phe Thr Gly Tyr Arg Ile Glu Leu Gln Ala 770 780

Cys Asn Gln Asp Thr Pro Glu Glu Arg Cys Ser Val Ala Ala Tyr Val

I

ALL MAN AND TANK

J

13

Ser Ala Arg Thr Met Pro Glu Ala Lys Ala Asp Asp Ile Val Gly Pro 805

Val Thr His Glu Ile Phe Glu Asn Asn Val Val His Leu Met Trp Gln 825

Glu Pro Lys Glu Pro Asn Gly Leu Ile Val Leu Tyr Glu Val Ser Tyr 840

Arg Arg Tyr Gly Asp Glu Glu Leu His Leu Cys Val Ser Arg Lys His 855

Phe Ala Leu Glu Arg Gly Cys Arg Leu Arg Gly Leu Ser Pro Gly Asn 875

Tyr Ser Val Arg Ile Arg Ala Thr Ser Leu Ala Gly Asn Gly Ser Trp 885 890

Thr Glu Pro Thr Tyr Phe Tyr Val Thr Asp Tyr Leu Asp Val Pro Ser 900 905

Asn Ile Ala Lys 915

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Leu Met Phe Thr Ala Thr Gly Glu Asp Phe Arg Gly Leu Ser Phe Pro

Arg Leu Thr Gln Val Thr Asp Tyr Leu Leu Leu Phe Arg Val Tyr Gly 55

Leu Glu Ser Leu Arg Asp Leu Phe Pro Asn Leu Ala Val Ile Arg Gly 70 75 80

Thr Arg Leu Phe Leu Gly Tyr Ala Leu Val Ile Phe Glu Met Pro His 85 90 95

Leu Arg Asp Val Ala Leu Pro Ala Leu Gly Ala Val Leu Arg Gly Ala
100 105 110

Val Arg Val Glu Lys Asn Gln Glu Leu Cys His Leu Ser Thr Ile Asp 115 120 125

Trp Gly Leu Leu Gln Pro Ala Pro Gly Ala Asn His Ile Val Gly Asn 130 135 140

Lys Leu Gly Glu Glu Cys Ala Asp Val Cys Pro Gly Val Leu Gly Ala 145 150 155 160

Ala Gly Glu Pro Cys Ala Lys Thr Thr Phe Ser Gly His Thr Asp Tyr 165 170 175

Arg Cys Trp Thr Ser Ser His Cys Gln Arg Val Cys Pro Cys Pro His
180 185 190

Gly Met Ala Cys Thr Ala Arg Gly Glu Cys Cys His Thr Glu Cys Leu 195 200 205

Gly Gly Cys Ser Gln Pro Glu Asp Pro Arg Ala Cys Val Ala Cys Arg 210 215 220

His Leu Tyr Phe Gln Gly Ala Cys Leu Trp Ala Cys Pro Pro Gly Thr 225 230 235 240

Tyr Gln Tyr Glu Ser Trp Arg Cys Val Thr Ala Glu Arg Cys Ala Ser 245 250 255

Leu His Ser Val Pro Gly Arg Ala Ser Thr Phe Gly Ile His Gln Gly 260 265 270

Ser Cys Leu Ala Gln Cys Pro Ser Gly Phe Thr Arg Asn Ser Ser Ser 275 280 285

Ile Phe Cys His Lys Cys Glu Gly Leu Cys Pro Lys Glu Cys Lys Val 290 295 300

Gly Thr Lys Thr Ile Asp Ser Ile Gln Ala Ala Gln Asp Leu Val Gly 305 310 315 320

Cys Thr His Val Glu Gly Ser Leu Ile Leu Asn Leu Arg Gln Gly Tyr 325 330 335

Asn Leu Glu Pro Gln Leu Gln His Ser Leu Gly Leu Val Glu Thr Ile 340 345 350

Thr Gly Phe Leu Lys Ile Lys His Ser Phe Ala Leu Val Ser Leu Gly 355 360 365

Phe Phe Lys Asn Leu Lys Leu Ile Arg Gly Asp Ala Met Val Asp Gly 370 380

Asn Tyr Thr Leu Tyr Val Leu Asp Asn Gln Asn Leu Gln Gln Leu Gly 385 390 395

Ser Trp Val Ala Ala Gly Leu Thr Ile Pro Val Gly Lys Ile Tyr Phe \$405\$ \$410\$ \$415\$

Ala Phe Asn Pro Arg Leu Cys Leu Glu His Ile Tyr Arg Leu Glu Glu 420 425 430

Val Thr Gly Thr Arg Gly Arg Gln Asn Lys Ala Glu Ile Asn Pro Arg 435 440 445

Thr Asn Gly Asp Arg Ala Ala Cys Gln Thr Arg Thr Leu Arg Phe Val 450 455 460

Ser Asn Val Thr Glu Ala Asp Arg Ile Leu Leu Arg Trp Glu Arg Tyr 465 470 475 480

Glu Pro Leu Glu Ala Arg Asp Leu Leu Ser Phe Ile Val Tyr Tyr Lys 485 490 495

Glu Ser Pro Phe Gln Asn Ala Thr Glu His Val Gly Pro Asp Ala Cys 500 505 510

Gly Thr Gln Ser Trp Asn Leu Leu Asp Val Glu Leu Pro Leu Ser Arg

515 520 525

Thr Gln Glu Pro Gly Val Thr Leu Ala Ser Leu Lys Pro Trp Thr Gln 530 535 540

Tyr Ala Val Phe Val Arg Ala Ile Thr Leu Thr Thr Glu Glu Asp Ser 555 560

Pro His Gln Gly Ala Gln Ser Pro Ile Val Tyr Leu Arg Thr Leu Pro 565 570 575

Ala Ala Pro Thr Val Pro Gln Asp Val Ile Ser Thr Ser Asn Ser Ser 580 585 590

Ser His Leu Leu Val Arg Trp Lys Pro Pro Thr Gln Arg Asn Gly Asn 595 600 605

Leu Thr Tyr Tyr Leu Val Leu Trp Gln Arg Leu Ala Glu Asp Gly Asp 610 615 620

Leu Tyr Leu Asn Asp Tyr Cys His Arg Gly Leu Arg Leu Pro Thr Ser 625 630 635 640

Asn Asn Asp Pro Arg Phe Asp Gly Glu Asp Gly Asp Pro Glu Ala Glu 645 650 655

Met Glu Ser Asp Cys Cys Pro Cys Gln His Pro Pro Pro Gly Gln Val
660 665 670

Leu Pro Pro Leu Glu Ala Gln Glu Ala Ser Phe Gln Lys Lys Phe Glu 675 680 685

Asn Phe Leu His Asn Ala Ile Thr Ile Pro Ile Ser Pro Trp Lys Val 690 695 700

Thr Ser Ile Asn Lys Ser Pro Gln Arg Asp Ser Gly Arg His Arg Arg 705 710 715 720

Ala Ala Gly Pro Leu Arg Leu Gly Gly Asn Ser Ser Asp Phe Glu Ile 725 730 735

Gln Glu Asp Lys Val Pro Arg Glu Arg Ala Val Leu Ser Gly Leu Arg
740 745 750

His	Phe	Thr 755	Glu	Tyr	Arg	Ile	Asp 760	Ile	His	Ala	Cys	Asn 765	His	Ala	A1a	
His	Thr 770	Val	G1y	Cys	Ser	Ala 775	Ala	Thr	Phe	Val	Phe 780	Ala	Arg	Thr	Met	
Pro 785	His	Arg	Glu	Ala	Asp 790	G1y	Ile	Pro	G1y	Lys 795	Va1	A1a	Trp	G1u	A1a 800	
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G1u	Ala	Thr 835	Va1	Leu	Cys	Va1	Ser 840	Arg	Leu	Arg	Tyr	A1a 845	Lys	Phe	Gly	
G1y	Va1 850	His	Leu	A1a	Leu	Leu 855	Pro	Pro	G1y	Asn	Tyr 860	Ser	A1a	Arg	Val	
Arg 865	Ala	Thr	Ser	Leu	Ala 870	Gly	Asn	Gly	Ser	Trp 875	Thr	Asp	Ser	Val	A1a 880	
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Leu Asn